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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,215	06/24/2003	Neema M. Kulkarni	PC 21501B	2258

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EXAMINER	
ANDERSON, JAMES D	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 06/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/602,215	KULKARNI ET AL.	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,16 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 18* is/are rejected.

7)☒ Claim(s) *16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Informalities

Claims 1-14, 16 and 18 are currently pending and are the subject of this Office Action.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 7, 2006 has been entered.

Claim Objections

Claim 16 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should only refer to preceding claims. See MPEP § 608.01(n). Accordingly, the claim has not been further treated on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-14 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/59573 in view of Zour *et al.* (Pharmaceutical Research, 1992, v. 9, pp. 595-600).

The '573 reference discloses solid and liquid pharmaceutical compositions comprising gabapentin analogs with increased stability (Abstract). The compositions further comprise amino acids that are disclosed as agents capable of inhibiting lactam formation (page 10, lines 1-12). Sweetening agents, such as mannitol and xylitol may also be added to the compositions "if needed" (page 41, lines 21-22).

Zour et al. disclose stability studies of gabapentin in aqueous solutions (Abstract). The reference demonstrates that the stability of gabapentin in aqueous solution is greatest at a pH of 6.0, and at 45 °C gabapentin demonstrated minimal degradation when formulated at a pH from 5.5 to 7.0 (see especially Fig. 6, page 598).

Thus, the instantly claimed compositions would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made. The motivation to combine the references can be found in Zour *et al.* wherein it is stated that in the pH range of 4.5 to 7.0, "the contribution of the uncatalyzed degradation rate constant would be highest, since the zwitterions are the predominant species in the solution in the aforementioned pH range" (p. 599, Col. 1). Given this disclosure, the skilled artisan would expect that formulations comprising gabapentin and having a pH from 5.5 to 7.0 would have inherent stability compared to formulations with a pH outside this range.

Applicants have argued that WO 99/59573 teaches away from the use of a polyhydric alcohol in pharmaceutical compositions containing a GABA analog. Applicant Response dated April 7, 2006. It is further argued that the specific limitation of a pH range of 5.5 to 7.0 is not disclosed by '573 and it is suggested by the applicants that the compositions of '573 were formulated at a pH outside the range of 6.0 to 7.3. In support of this argument, a Declaration under 37 C.F.R. § 1.132 was submitted by Dr. Mei Cai. The declaration has been carefully considered but is not persuasive for the reasons given below.

In Table 4, Sample (e) of the WO 99/59573 reference, the composition comprises 5% gabapentin and 15% xylitol. This corresponds to Formulation B in Tables 1 to 4 of the Cai Declaration. After one week of storage at 45 ^{o}C, Sample (e) of the reference contained 0.311% lactam. The corresponding formulation in the Cai Declaration had 0.343% lactam when formulated at a pH of 5.5 and kept under the same conditions. After 2 weeks, Sample (e) of the reference had 0.616% lactam

compared to 0.677% in Formulation B of the Cai Declaration. No data is available for Formulation B at a pH of 5.5 in Week 3 but it is noted that Sample (e) of the reference contained 0.947% lactam after 3 weeks at 45 °C. If the reference formulations were at a pH of below 5.5, one would expect there to be more lactam formation than is actually observed. However, the observed 0.311% lactam formation after 1 week of storage at 45 °C in the reference corresponds with the 0.343% observed in the Cai disclosure at a pH of 5.5 (Table 2, Sample B, pH = 5.5). It is also apparent that at a pH of about 5.5, the presence of 15% xylitol appears to have little to no effect on lactam formation in the compositions (compare, for example, Formulations A and B at pH 5.5 after 1 and 2 weeks of storage). Declaration, p. 5, Tables 1 and 2.

Applicants further argue that, with regard to Table 4 in the reference, the statement that degradation could be prevented "by the addition of glycine even in the presence of xylitol," it is meant that degradation is prevented despite the presence of xylitol. Applicant Response, page 7. This argument is not persuasive because glycine prevents degradation of the composition even when xylitol is not present (compare, for example, Samples (d) and (f) in Table 4). It is noted that the "comprising" language of the present claims allows for the presence of both xylitol and glycine. It is further noted that the '573 reference discloses that a sweetening agent such as xylitol may be present in the compositions. Thus, it is the Examiner's position that the applicants of the '573 reference are simply stating that the stabilizing effect of glycine is unaffected by the presence of the sweetening agent in the composition, *i.e.* glycine maintains its stabilizing effect in the presence of xylitol. Support for this position is found in the '573

document on page 40, lines 3-5 wherein it is stated that, "...there may be incorporated, if required, a sweetening agent and/or a flavoring agent, which do not influence on the effect of the amino acid stabilizer." Thus, '573 does not teach away from compositions comprising gabapentin analogs and xylitol as instantly claimed.

Table 5 (p. 46) of the reference discloses formulations comprising 5% gabapentin, 20% xylitol, 1.65% glycine, and 1.95% DL-alanine (Sample (h)). It is clear that these formulations demonstrate reduced lactam formation at elevated temperatures for 2-6 weeks as well as decreased temperatures for 6 to 12 months. It is noted that the "comprising" language of the instantly claimed compositions allows for the presence of glycine and DL-alanine as disclosed in '573.

As stated *supra*, the instantly claimed pH range would have been obvious to the skilled artisan given the disclosure of Zour *et al.* Thus, the combined references teach all of the limitations of the instantly claimed invention.

In determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); *Schenck v. Nortron Corp.*, 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983). As discussed *supra*, it is the Examiner's position that the instantly claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

James D. Anderson
Examiner
Art Unit 1614

June 12, 2006

6/15/06

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER